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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/582,176	04/18/2007	Kiyotaka Nakano	14875-0163US1/C1-A0322P-U	8936

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EXAMINER	
DO, PENSEE T	

ART UNIT	PAPER NUMBER
1641	

NOTIFICATION DATE	DELIVERY MODE
10/29/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

PATDOCTC@fr.com

Office Action Summary	Application No.	Applicant(s)	
	10/582,176	NAKANO ET AL.	
	Examiner	Art Unit	
	Pensee T. Do	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 July 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *6-11 and 15-24* is/are pending in the application.

4a) Of the above claim(s) *6-11* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *15-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *6-11 and 15-24* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/14/2010; 9/1/2010; 7/23/2010; 8/5/2009; 1/20/2009*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application.
6) ☐ Other: _____.

DETAILED ACTION

Priority

Application 10582176, PG Pub. No. 20070281327, filed 04/18/2007 is a national stage entry of PCT/JP04/18499, International Filing Date: 12/10/2004 and claims foreign priority to 2003-415733 , filed 12/12/2003.

Information Disclosure Statement

IDS papers submitted on July 23, 2010; September 1 and September 14 have been acknowledged and considered.

Regarding the IDS paper filed on August 5, 2009, page 4 is not signed.

Regarding the IDS paper filed on January 20, 2009, the citing Tawara is now considered.

Amendment Entry & Claims Status

The amendment filed on July 23, 2010 has been acknowledged and entered.

Claims 1-5, 12-14 are canceled.

Claims 6-11 are withdrawn.

Newly added claims 15-24 are pending and being examined.

Withdrawn Rejection(s)

Rejection under 112, 2nd paragraph in the previous office action is withdrawn herein.

Rejection under USC 102(e) for claims 1-5, 12-14 in the previous office action is withdrawn herein.

Claimed Invention

15. (New) A method of screening comprising:

(a) providing a plurality of whole antibodies that bind to a given antigen, wherein the plurality of whole antibodies comprises antibodies with weak or undetectable agonistic activity for the antigen;

(b) producing a minibody of each whole antibody;

(c) screening the minibodies for their ability to agonize the antigen; and

(d) selecting a minibody if it exhibits agonistic activity greater than that of its respective whole antibody.

Maintained Rejection(s)

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321© or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 15-24 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 40-42, 55, 59 of copending Application No. 10/582,413. Although the conflicting claims are not identical, they are not patentably distinct from each other because copending application '413 claims the a method of screening for an agonist antibody comprising the steps of identifying an antibody that binds to a receptor; modifying the antibody; and determining the agonist activity of the modified antibody and selecting modified antibody with agonist activity.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

New Grounds of Rejection

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 15-17, 19-22 and 24 are rejected under 35 U.S.C. 102(e) as being anticipated by Fukushima et al. (US PG Pub. No. 2004/0242847 submitted by Applicants in IDS 4/23/2007).

For claim 15, Fukushima teaches a method of screening for an agonist antibody comprising the steps of: providing a plurality of whole antibodies that bind to a given antigen, wherein the plurality of whole antibodies comprise antibodies with weak or undetectable agonistic activity for the antigen; producing a minibody of each whole antibody; screening the minibodies for their ability to agonize the antigen; and selecting the minibody if it exhibits agonistic activity greater than that of its respective whole antibody. (see entire document; e.g. [231]; (see example 6); [0281]-[291]; [324]; [325]; [369]).

Regarding claim 16, Fukushima teaches the antibody is against protein expressed on cell membrane. (see [034]).

Regarding claim 17, Fukushima teaches the antigen is a receptor. (see [325]).

Regarding claim 18, Fukushima teaches the antigen is Leukemia inhibitory factor LIF receptors. (see [0035]).

Regarding claim 19, Fukushima teaches the antigen is a thrombopoietin (TPO). (see [0325]).

Regarding claim 20, Fukushima teaches the antigen is CD47 (see [0035]).

Regarding claim 21, Fukushima teaches the modified antibody is sc(Fv)2. (see [230]).

Regarding claim 22, Fukushima teaches the minibodies are diabodies. (see [0061]).

Regarding claim 23, Fukushima teaches the agonist activity is not determined before the antibody is modified. (see example 6; and [324] and [325]).

Regarding claim 24, Fukushima teaches that the plurality of whole antibodies is together in a mixture. (see [0325]).

Response to Arguments

Applicant's arguments filed July 23, 2010 have been fully considered but they are not persuasive.

Regarding the new abstract filed on July 23, 2010, it has been acknowledged and entered.

Regarding the IDS, all the requests are fulfilled and please see attached considered IDS.

Regarding the ODP rejection, although claims 1-4, 12-14 are cancelled. The rejection is still applicable to the newly added claims. Therefore, it is still maintained.

Regarding the 102 (e) rejection by Fukushima, Applicants argue that:

Fukushima fails to teach a plurality of whole antibodies that bind to a given antigen wherein the plurality of whole antibodies comprises antibodies with weak or undetectable agonistic activity for the antigen. Applicants submit that Fukushima describes experiments with three different whole antibodies, two of which (12B5 and 12E10) bind to MPL and another of which (MABL-2) binds to a different antigen (CD47). Of the three antibodies, the only plurality of whole antibodies that bind to a given

antigen is the "plurality" made up of 12B5 and 12E10, both which bind MPL. Fukushima discloses that one of those two whole antibodies has weak or undetectable agonistic activity for MPL.

This is not found persuasive because:

In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., a plurality of "different" whole antibodies) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Claim 15 requires " a plurality of whole antibodies", NOT "a plurality of ***different*** whole antibodies". Applicants are arguing for a limitation that is not in the claim. C

Fukushima teaches the agonistic activity to MPL is measured using culture supernatants of COS-7 cells expressing various 12E10 antibody molecules and the results are shown in Figure 58. Thus, in a culture supernatant of cells expressing various 12E10 antibody molecules, which includes whole antibody 12E10 IgG molecules, there must be more than one or a plurality of 12E10 IgG whole antibody molecules since there is a plurality of cells being used.

Applicants also argue that the list of antigens in claim 18 does not include MPL.

This is not found persuasive because Fukushima does teach other receptors such as leukemia inhibitory factor (LIF) receptors. (see [0035]).

Applicants further submit that Fukushima fails to teach claim 23, which requires that the agonistic activities of the whole antibodies are not assayed prior to step (b) of claim 15 which is the step of modifying the whole antibodies.

This is not found persuasive because:

Fukushima performs side-by-side assays on each whole antibody and its minibody forms [0324]; [0325]. Thus, the agonistic activity of the whole antibody is performed after the minibody is formed so that side-by-side assays are performed to compare the agonistic activities.

Applicants further argue that Fukushima fails to teach claim 24 which requires that the plurality of whole antibodies are in a mixture and pointed to examples 6,7, and 8 in Fukushima showing that the whole antibodies (MAL-2, 12B5, and 12E10) are handled separately and they are not in a mixture.

This is not found persuasive because:

Again, the claims 15 and 23 do not require that the plurality of whole antibodies is "different" antibodies. Therefore, this argument is irrelevant.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within

TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Pensee T. Do whose telephone number is 571-272-0819. The examiner can normally be reached on Monday-Friday, 9-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mark Shibuya can be reached on 571-272-0806. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Pensee T. Do/
Examiner, Art Unit 1641
/Jacob Cheu/
Primary Examiner, Art Unit 1641